



Diagnosis and Management of Early Stage Diabetic Kidney Disease

1. Jamal Ahmed Abdul-Barry

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¹ Department of Biochemistry, Faculty of Medicine, University of Basrah

Mobil: 07802829835

e-mail: Aldohan57@yahoo.com

Abstract: Background: Diabetes mellitus causes the majority of end-stage renal impairment that necessitates replacement in order to survive. Cardiovascular morbidity and death increase with diabetic renal disease. Early detection and therapy can halt the course of renal disease. This case-control study investigated the clinical significance of serum creatinine, blood urea, and eGFR in predicting renal impairment and assessing renal function in normoalbuminuric and microalbuminuric type 2 diabetics.

Methodology: From October 2021 to June 2022, a 9-month case-control study divided 70 patients with type 2 diabetic renal impairment admitted to the Private Clinic Laboratory of Basrah, aged 40 to 68 (24 males and 46 females), into three groups (mild, moderate, and severe renal impairment) based on their signs and symptoms. Alternatively, 60 healthy participants (28 men and 32 women) were recruited. Participants in the control group ranged in age from 40 to 70 years old. Sugar, HbA1c, Urea, Creatinine, albuminuria, and e GFR were measured in venous blood samples from research participants using standard procedures.

Results; When compared to controls, patients with type 2 diabetes exhibited significantly higher mean values of fasting blood glucose, glycated hemoglobin, blood urea, and serum creatinine (P 0.05) and non-significantly lower eGFR (p > 0.05). The study discovered that 45.7% of individuals had poor glycemic control (HbA1c% 8.5) and were treated in a variety of ways: 10% with insulin therapy, 62.85% with oral

hypoglycemic medications, 12.85% with both, and 14.3% with simply a regulated diet. 43.6% of diabetics had a family history of Type 2 diabetes. There were significant ($P < 0.05$) changes in DM duration, B. Urea, S. Creatinine levels, and GFR between normoalbuminuric and microalbuminuric type 2 diabetic patients, but no differences in age, FBS, or HbA1c. In a study of 33 microalbuminuric patients, 12 were classified as stage 1 (eGFR (90-90) mL/min/1.73 m²), 10 as moderate (eGFR (60-90) mL/min/1.73 m²), and 11 as severe.

Conclusions: Elevated serum creatinine and blood urea, as well as a decline in eGFR, predict renal impairment in normoalbuminuric type 2 diabetes. Diabetic nephropathy rates rose due to poor glycemic control. Albumin and/or reduced eGFR (60 mL/min/1.73m²) were seen in patients.

Key words: Diabetes, renal impairment, Sugar, HbA1C, Urea, Creatinine, albuminuria, eGFR.

INTRODUCTION

Diabetes's mellitus (DM) is the leading cause of chronic kidney disease (CKD) worldwide. CKD occurs in 20-40 % of patients suffering from diabetes (1).

A number of patients with diabetic kidney disease (DKD) ultimately culminate into end stage kidney disease (ESKD). To sustain life, the treatment of ESKD needs renal replacement therapy (RRT) which includes dialysis or kidney transplantation (2, 3).

The prevalence of ESKD due to diabetes is increasing due to continued rise in the number of type 2 diabetes (T2D) worldwide (1).

On the other hand diabetic nephropathy is most relevant chronic progressive complication result from long-term microvascular complications of diabetes in terms of morbidity and mortality (I.e., angina, unstable angina, myocardial infarction, peripheral arterial disease, stroke and death) and is the leading cause of ESRD (4,5,6,7).

There is strong evidence that a number of interventions if initiated at an early of DKD, reduce the risk and slow the progression to ESKD, and decrease CV morbidity and mortality (8).

Therefore, early diagnosis and management of DKD is important. The management of those factors responsible for development and progression of ESKD and CV events have been discussed.

Methodology

A case control study was conducted over a 9-month period, from October 2021 to June 2022, in which 70 patients with various types of type 2 diabetic renal impairment who were admitted to the Private Clinic Laboratory of Basrah, their ages ranging from 40 to 68 years olds (24 males and 46

females), were divided into three groups (mild, moderate, and severe renal impairment) based on their symptoms and duration of illness and kept on different medications. In contrast, there were 60 apparently healthy subjects (28 males and 32 females). As a control group, they ranged in age from 40 to 70 years old. For measurements, venous blood samples were taken from each subject and patient who took part in this investigation. Sugar, HbA1C, Urea, Creatinine, ACR ratio, eGFR, and urine samples were collected for standard albuminuria measurement.

Statistical Analysis

Statistical analysis was done by chi-square test, student's t-test, and the logistic regression. The results were expressed in the form of men \pm standard deviation. using SPSS (version 26).

Results

The baseline clinical characteristics of the patients and control groups are shown in **Table 1:**

Table 1. Showed that the study population consists of 70 patients with type 2 diabetes mellitus allocated into three groups mild, moderate and severe renal impairments (24 male and 46 female) with mean age of (58.6 ± 10.7) years, compared to 60 apparently healthy adult (28 male and 32 female) with mean age of (57.0 ± 11.3) years representing the control group, the differences was statistically not significant ($P = \text{value} > 0.05$). The mean systolic blood pressures were $140.2 (\pm 21.4)$, $116.7 (\pm 6.72)$, mean diastolic blood pressures were $85.4 (\pm 10.6)$, $79.1 (\pm 6.3)$ for patients and control groups respectively.

The differences for both systolic and diastolic blood pressure were statistically significant (P value < 0.05). Most of them were nonsmokers. Also the comparison between 3 renal impairment groups (mild, moderate and severe) were statistically not significant (P value > 0.05) regarding mild and moderate groups.

Table 1. Clinical characteristics of the study population

Clinical characteristic		Patients N=70	Controls N=60	P value *
Age(yr)		58.6 (± 10.7)	57.0 (± 11.3)	0.337
Sex (M/F)		(24/46)	(28/32)	
Systolic Blood pressure (mm Hg)		140.2 (± 21.1)	116.7 (± 6.72)	0.000
Diastolic Blood Pressure (mmHg)		85.4 (± 10.6)	79.1 (± 6.3)	0.000
Stage 1 with (eGFR > 90 mL/min/1.73 m ²), Mild.		12 (± 0.66)	0.81 (± 0.52)	0.000
Stage 2 with (eGFR (60-90) mL/min/1.73 m ²), Moderate.		10 (± 5.01)	0.43 (± 5.7)	0.001
Stage 3 with (eGFR (30-60) mL/min/1.73 m ²), Sever		11 (± 8.1)	0.26 (± 5.7)	0.02
Smoking behavior	Smoker	16.3 %	4.4 %	
	Non-smoker	84.7 %	95.6 %	

Value is expressed as mean \pm SD

* P value <0.05 was considered statistically significant.

The means of biochemical parameters measured in this study for both patient and control groups are shown in the Table 2:

Table 2. Showed that the mean values of fasting blood glucose (FBG), glycated hemoglobin (HbA1c), blood urea (B. Urea) and serum creatinine (s. Creatinine), were higher as compared with that of the control group. The difference was statistically significant. (P value <0.05). eGFR of diabetic patients differ from that of control group but they did not reach to the degree of statistical significance (P value >0.05).

The clinical characteristics of 70 type 2 diabetic patients presented in the

Table 2. Biochemical parameters in study population

Parameters	Patients	Control	P value*
	N=70	N=60	
FBG (mg/dl)	163.2 (\pm 63.1)	102.0 (\pm 12.3)	0.000
HBA1c (%NGSP)	9.23 (\pm 1.4)	5.40 (\pm 0.83)	0.000
B. Urea (mg/dl)	43.7 (\pm 25.6)	24.8 (\pm 5.26)	0.000
S. Creatinine(mg/dl)	1.10 (\pm 0.67)	0.72 (\pm 0.27)	0.003
e GFR (ml/min/1.73 m2)	91.5(+39.5)	98.5 (+25.6)	0.32

Table 3. The Basic Characteristics of type 2 diabetic patients

Characteristic		N	%	mean \pm SD
Age (years)		70		58.6 \pm10.6
Age group	<40 yr	10	14.3%	34.6 \pm 5.5
	40-65 yr	51	72.85%	55.5 \pm 6.5
	\geq 65 yr	9	12.85%	71.8 \pm 6.2
Sex	Male	24	34.28%	-----
	Female	46	65.71%	-----
Duration of diabetes (year)		70		9.2 \pm8
Duration of diabetes group	\leq 10 yr	48	68.6%	4.60 \pm 2.5
	>10 yr	22	31.4%	18.17 \pm 9.0
Family history of Type 2 diabetes	Positive	43	61.4 %	-----
	Negative	27	38.6%	-----

Blood pressure SBP/DBP (mm Hg)		70		140.2 ±21.4/85.6 ±10.6
BP (SBP/DBP) mm Hg	Controlled BP (<130/80 mm Hg)	43	61.4%	-----
	Uncontrolled BP (≥130/80 mm Hg)	27	38.6%	-----
HbA1c		70		9.2 3±1.4
HbA1c groups	HbA1c %<6.5	17	24.3%	6.25±0.6
	HbA1c % 6.6-8.4	21	30.0%	8.21±0.6
	HbA1c %≥8.5	32	45.7%	12.5±1.3
Type of diabetic treatment	Insulin	7	10.0%	-----
	Oral anti-hyperglycemic drug	44	62.85%	-----
	Both	9	12.85%	-----
	No drug treatment (controlled diet)	10	14.3%	-----

Table 4: The Classification of Diabetic Patients According To Albuminuria

The patients with type 2 diabetes involved in the study had been allocated into 2 groups regarding the presence or absences albuminuria for the urine albumin/creatinine ratio (ACR) (mg/g creatinine). These two groups are Normoalbuminuria (ACR <30 mg/g creatinine) and Microalbuminuria (ACR 30–300 mg/g creatinine), as shown in Table 4.

Diabetic patients ACR (mg/g creatinine)		N	%	mean ± SD
Albuminuria groups	Normoalbuminuria	37	52.85 %	24.28±53.2
	Microalbuminuria	33	47.3 %	213.8±61.1
All groups		70	100%	119.04± 57.1

Value are expressed as mean ± SD or number (%).

This study demonstrates that the mean ACR of all patients was (119.04±57.1). 52.85% were found to have normoalbuminuria, and 47.3 % were found to have microalbuminuria.

Table 5. The Clinical and biochemical characteristics of 70 patients with type 2 diabetes according to albuminuria groups.

On the other hand, Table 5. Have been shown the Clinical Data Parameters in Patients with Type 2 Diabetes and their Classification on The Basis of Albumin Excretion Rate. The Table revealed that, there were no significant differences in age, FBS, HbA1c, between the normoalbuminuria and microalbuminuria groups with (P value>0.05). However, there were significant statistically difference in the DM duration. B. Urea, S. Creatinine levels, eGFR and ACR between the 2 groups with (P < 0.05).

Parameters	Normoalbuminuria N=37	Microalbuminuria N=33		*P value
Age (yr)	52.85 (±9.98)	47.3 (±13.12)		0.184
DM Duration (yr)	7.26 (±3.6)	11.3 (±9.5)		0.003
FBS (mg/dl)	161.6 (±83.55)	163.7 (±61.34)		0.136
SBP (mm Hg)	140.86(±21.9)	141.4(±23.25)		0.41
DBP (mm Hg)	84.95(±7.0)	86.80(±12.2)		0.33
HBA1c%	9.11 (±2.51)	9.31 (±2.43)		0.672
B. Urea(mg/dl)	41.25 (±11.90)	46.24 (±19.77)		0.010
S. Creatinine (mg/dl)	0.93(±0.19)	1.12 (±0.60)		0.001
eGFR (mL/min/1.73 m ²)	102.34(±38.13)	81.32(±34.37)		0.001
ACR (mg/g)	24.28(±53.26)	213.8(±61.1)		0.001

Value are presented as mean± standard deviation

*p value <0.05 consider statistically significant

Discussion

Diabetes mellitus is a major worldwide health problem and DKD is one of the most important complication of both type 1 and T2D. Analysis of data from the US national representative data system revealed that among the diabetes – related complication there was the smallest decline in ESRD as compared with acute myocardial infarction, hyperglycemic crisis, stroke and lower –extremity amputation (1, 8,9,10).

The decline of most of the diabetes – related complications may reflect a combination of advances in clinical care, enhanced management of risk factors, and improvement of health promotion efforts directed at patients with diabetes (8, 9, 10).

Currently, there are substantial number of guidelines around the world to management DKD at the national and international levels. In the various guidelines there are certain controversies and differences in diagnosis and management of DKD (9, 10).

However, all the guidelines concur with the basic recommendations in the management of DKD (11, 12).

From the data collected in this study, diabetic patients were female-dominant, the mean age of diabetic patients was 58.6±10.7 years which is close to other researches (11, 12) and slightly higher than the mean age reported (13, 14).

The study showed that the mean duration of studied patients with type 2 diabetes since diagnosis was 9.2±8 years and 61.4% of the patients had family history of diabetes which is close to result obtained by (13) and higher than percentage of other researches(14, 15) .

Regarding treatment of studied patients they were kept on different modalities of treatment. Only 10 % of patients kept on insulin, due to that our patients are false believes of using insulin therapy (16, 17). In comparison with other studies 42.4% were kept on insulin treatment (18, 19).

In this study the mean of blood pressure (SBP/DBP) was $140.2 \pm 21.1 / 85.4 \pm 10.6$ mm Hg and is considered hypertensive range in diabetic patients. The result is higher than that reported by others (20). Blood pressure was controlled ($<130/80$ mm Hg) at the time of visit in only 43.61% of diabetic patients that means approximately more 1/4 of patients of our patients have uncontrolled blood pressure. Hypertension is considered as a complication of long standing diabetes mellitus in particular for those with diabetic nephropathy and hypertension itself considered as risk factor for progression of diabetic nephropathy (21, 22, 23).

The mean fasting blood glucose level of the diabetic patients was $163.23 (\pm 63.1)$ mg/dL, which was relatively high. The mean HbA1c was $9.23 \pm 1.4\%$. most of the diabetic patients were in uncontrolled hyperglycemic state and only 24.3% of 70 patients achieved goal glycemic control (HbA1c $< 6.5\%$) in comparison with other study were 56.1% achieved goal glycemic control (24, 25) and probably these high figure of HbA1c in the patients because of the poor follow up and poor compliance to anti-diabetic medication and so reflecting the higher rate of complication including diabetic nephropathy in our locality. For many years microalbuminuria is still the most popular method used as a predictor of incipient DNP (26).

In the present study the mean of ACR was 24.28 mg/g in the normoalbuminuria diabetic group; while in diabetic microalbuminuria group it was 213.8 mg/g which is statistically significant difference (P value < 0.05) which reflects kidneys involvement of diabetic patients. This result is in consistent with other studies (27, 28). This study showed that 52.85% of the diabetic patients had normo albuminuria and 47.14% had microalbuminuria. This indicates that approximately 1/3 of the studied diabetic patients had abnormal ACR, which is in agreement to that results obtained (29, 30, While higher than that reported in population-based studies of diabetic patients in other area (31, 32, 33, 34). Such variation probably can be explained by many factors like sample collection, assessment of microalbuminuria, duration of diabetes, raised blood pressure, poor glycemic control and educational level (35). FPG, HbA1c also showed no statistically significant differences (P value < 0.05) in present study between two normoalbuminuric and microalbuminuric groups in contrast to the results obtained by others (36). This could be explained; in the present study the mean HbA1c was high while in the comparing literatures, it was relatively controlled (37).

Diabetic duration was longer in microalbuminuria groups than normo albuminuria group with statistically significant difference (P value < 0.05) between these two groups. Same results were obtained by (38) where the duration of diabetes was considered as strongest predictor of increased ACR. The serum levels of urea and creatinine were elevated significantly in those with high ACR level (p value < 0.05), while eGFR was significantly lower in those with high ACR level (p value < 0.05) similar to that result obtained by others (39, 40, 41, 42).

By analyzing the present results, it could be conclude that the DKD usually progresses to ESKD, it is also a risk for CV morbidity and mortality. Early diagnosis and management with multifactorial interventions is important to reduce the progression of early DKD to ESKD and also to reduce the risk

of CV events. Among the ant-diabetic agents which have been reported to improve renal outcomes by reducing the amount of albuminuria and preventing GFR loss in patients with T2D.

Conclusion:

Patients with normoalbuminuric type 2 diabetes who exhibit elevated levels of serum creatinine and blood urea, along with a decline in estimated glomerular filtration rate (eGFR), can be considered as indicators for the progression of renal impairment. The rise in the incidence of diabetic nephropathy can be attributed to inadequate glycemic control. The patients exhibited either the presence of albumin or a reduced estimated glomerular filtration rate (eGFR) of 60 ml/min/1.73m², both of which fell below the established normal limit.

The objective of this study is to investigate the potential association between diabetes and renal impairment. Specifically, our study aims to examine the impact of sugar consumption on various biomarkers, including HbA1C levels, urea levels, creatinine levels, albuminuria levels, and estimated glomerular filtration rate (eGFR).

Ethical considerations check and revise to your information

Written illustrative consent form was signed by all parents/caregivers of the participating patients. This study was performed according to the ethical rules for medical research involving human participants of the Declaration of Helsinki (1964). Ethical approval was received from the ethical and research committee of Department of Biochemistry, Faculty of Medicine, University of Basrah.

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